

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

On Re the Application of:

HOWELL et al.

Serial No.: 09/444,144

Filed: November 20, 1999

Attorney File No.: 4369-1  
(formerly Cyto001)

For: METHOD FOR ENHANCING  
IMMUNE RESPONSES IN  
MAMMALS

Group Art Unit: 1642

Examiner: Helms, L.

DECLARATION OF  
MARK D. HOWELL,  
CHERYL L. SELINSKY AND  
LELAND C. LEBER  
(37 CFR § 1.131)

Assistant Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

We, Mark D. Howell, Cheryl L. Selinsky and Leland C. Leber, each declare as follows:

1. I am a co-inventor of the above-referenced patent application and am familiar with the application.

2. This Declaration under 37 CFR 1.131 is being submitted in conjunction with an Amendment and Response to an Office Action having a mailing date of August 10, 2001.

3. This Declaration provides factual evidence that the invention as claimed in the above-identified patent application was conceived of prior to the earliest priority filing date of U.S. Patent No. 6,231,536, followed by diligence in reduction to practice from a date prior to the earliest priority filing date of U.S. Patent No. 6,231,536, to the filing date of the above-identified patent application. All acts relied upon to establish the dates of conception, diligence and constructive reduction to practice were carried out in the United States.

a. *Conception:*

The invention presently claimed in the above-identified patent application was conceived of prior to May 22, 1998, which is the earliest priority filing date for U.S. Patent No. 6,231,536. As evidence of conception by a date prior to May 22, 1998, enclosed as

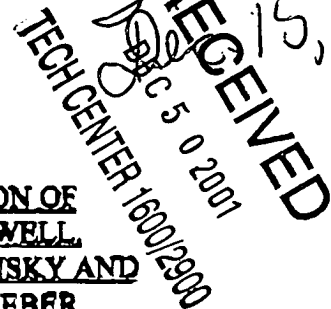


Exhibit A is a Project Summary that was included in a letter from coinventor Mark Howell to an individual who was a potential source of research funding. This letter sets forth the concept as claimed in the present invention, and it proposed experiments to begin reduction to practice of the invention. This letter was written and prepared at a date prior to May 22, 1998.

Specifically, the letter and Aim 6 indicate that the proposal is a description of a project to be performed in canines, which is a prelude to human clinical trials. Aim 2 of the proposal outlines the experimental plan to purify soluble tumor necrosis factor receptor (sTNFR) and to develop monoclonal antibodies against sTNFR. Aim 4 of the proposal describes the coupling of anti-sTNFR antibodies to a solid support to produce immunosorbent matrices. These immunosorbent matrices are to be tested for their ability to "efficiently deplete sera and ultrafiltrates...of sTNFR." Aim 5 describes the proposal to incorporate the immunosorbent matrices into existing ultrapheresis technology to deplete the ultrafiltrate of sTNFR, thus allowing reinfusion of the ultrafiltrate." Aim 6 describes how the immunosorbent matrix will be incorporated into an ultrapheresis device. Aim 6 also describes the plan to develop and test immunosorbent methods for the removal of other inhibitors of the immune system and to begin clinical trials in human patients.

This evidence is believed to be sufficient to establish conception of the presently claimed invention at a date prior to May 22, 1998.

b. *Diligence:*

Diligence in reducing the claimed invention to practice began prior to May 22, 1998. Exhibit B and its attachments demonstrate diligence in reduction to practice from prior to May 22, 1998 to November 20, 1999, the latter date being the filing date of the application and therefore, the date of constructive reduction to practice. Specifically, Exhibit B is a chart that describes, using ranges of dates from November 14, 1997 to November 20, 1999, experiments performed in each date range that pertained to the reduction to practice of the claimed invention. Exhibit B also references attached notebook pages that describe certain experiments conducted during the specified period and which document the completion of experiments describing reduction to practice of the present invention.

This evidence is believed to be sufficient to establish due diligence from a period prior to May 22, 1998, to the constructive reduction of the invention to practice on November 20, 1999.

c. *Constructive Reduction To Practice:*

The above-identified patent application was filed on November 20, 1999, which is the date of constructive reduction to practice.

4. I hereby declare that all statements made herein of my own are true and that all statements made on information and belief are believed to be true; and further that the statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the subject application or any patent issuing therefrom.

10/22/01  
Date

Mark D. Howell  
Mark D. Howell

10/22/01  
Date

Cheryl L. Selinsky  
Cheryl L. Selinsky

10/22/01  
Date

Leland C. Leber  
Leland C. Leber